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Eliminating the Suffering and Death Due to Cancer

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Report to the Nation: Trends in Cancer Treatment

The overall cancer death rate in the United States continues to decline while the overall rate of newly diagnosed cases is essentially unchanged, according to the *Annual Report to the Nation on the Status of Cancer*. The report includes data on cancer mortality and incidence from 1975 through 2002, the most recent year for which statistics are available.

The trend of declining cancer death rates has occurred as physicians in community settings have increasingly adopted treatments recommended by leading cancer organizations and professional societies, according to the study. The researchers used data from NCI's SEER (Surveillance, Epidemiology, and End Results) cancer registries and related resources to track treatments throughout the population over time.

But not all racial and ethnic groups have benefited equally from the progress. The researchers found disparities in the quality of care available in minority and underserved communities as compared with others. They also found different patterns of treatment for cancers, depending on geography.

The study's data "raise substantial concerns" that a patient's treatment may depend on nonclinical factors such as

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Director's Update

Even with Changes, NCI Always Moving Forward

Last week brought with it an important change at the National Cancer Institute (NCI), with my appointment as interim commissioner of the Food and Drug Administration (FDA) by President Bush. And as I said at the time, I will maintain my position as NCI director and my ultimate commitment to the 2015 goal.

To ensure that the many ambitious initiatives and programs we have launched to reach that goal continue to progress, Department of Health and Human Services Secretary Mike Leavitt has asked Dr. John Niederhuber, who recently came to NCI as deputy director for translational and clinical sciences, to serve as the NCI chief operating officer to handle much of the institute's day-to-day management.

These changes come just as NCI releases the *Report to the Nation*, which contains excellent news: Death rates from cancer are continuing to fall, albeit modestly.

As this encouraging trend demonstrates, it has never been more important to ensure that NCI has stable leadership, and I'm confident that Dr.

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(Trends continued from page 1)
race, socioeconomic status, age, and where the patient lives, the researchers write in the October 5 *Journal of the National Cancer Institute*.

"We do find that lower income and minority patients and older individuals do not appear to be getting recommended treatments at optimal rates," says co-author Dr. Martin L. Brown of NCI's Division of Cancer Control and Population Sciences (DCCPS). "That sends an important message to the community and reminds people that we should make sure treatment is being delivered appropriately."

Dr. Brown points out that some "patients may not be getting the recommended treatments for appropriate reasons, such as coexisting medical conditions." The data do not indicate why patients were given one treatment over another.

An example of treatment recommendations affecting patients broadly has been the substantial increase of women with early-stage breast cancer receiving breast-conserving surgery with radiation treatment. The increase was triggered by a 1990 National Institutes of Health (NIH) Consensus Development Panel report that this surgery followed by radiation is as effective as mastectomy but preserves the breast.

The researchers note, however, that recommendations are not always followed completely. For instance, there has been a modest but increasing use of breast-conserving surgery *without* radiation to treat women with early-stage breast cancer.

The report also updates statistics on the nation's cancer burden. A change from last year's report was a small increase in the overall lung cancer death rate among women for the period 1995 to 2002.

"The good news is that the decline in overall cancer death rates is being driven by declines in many cancers," says first author Dr. Brenda K. Edwards, also of NCI's DCCPS. Death rates are down for 12 of the top 15 cancers in men, and 9 of the top 15 cancers in women.

Nevertheless, the absolute total number of cancer deaths has actually increased, which the researchers attribute to the growing number of older Americans.

The incidence rate for all cancers combined among men was stable from 1995 through 2002, but the rate among women increased by 0.3 percent annually from 1987 through 2002. "The lung cancer incidence rate in women is finally stabilizing, suggesting that declines may occur in the future," notes Dr. Edwards.

The annual report, first published in 1998, is a collaborative effort of the American Cancer Society, the Centers for Disease Control and Prevention, NCI, and the North American Association of Central Cancer Registries. ◆

By Edward R. Winstead

(Director's Update continued from page 1)

Niederhuber, in cooperation with the superb NCI senior leadership team, will ensure that our vital work continues unabated. Without minimizing the significance of any mortality decline, it is important to note that we are engaged in numerous initiatives and programs that I believe have the potential to deliver precipitous declines in death rates.

This potential is largely rooted in our investment in advanced technologies. Indeed, we have roared into the era of molecular oncology with a diverse array of technological tools—microarrays, proteomics, nanotechnology, and advanced imaging devices and agents, to name just a few—that are becoming bedrocks of the discovery-development-delivery continuum.

We have used this technology to advance our understanding of the role of genetics in cancer, as we move closer to a time when new drugs are developed concurrently with genetic tests that will greatly improve the likelihood of a given agent benefiting a particular patient. Proteomics holds the great promise of aiding the development of diagnostic tests that can catch cancers or recurrence at the earliest stages. Nanotechnology and advanced imaging devices are moving us toward novel ways for accurately delivering treatments and assessing in real time whether they are having their desired effect. And in the midst of all this is the continued development of the cancer Biomedical Informatics Grid, which promises to offer new, effective tools for conducing research, while fostering the movement toward team science.

Obviously, NCI is not the only player in these efforts, all of which make up a massive undertaking that involves thousands upon thousands of committed researchers, advocates, policy makers, and, clearly, regulatory bodies like FDA.

While their missions may differ somewhat, NCI and FDA, along with the other government health agencies, share a common goal of improving public health. I am committed to leading FDA through this time of transition and fulfilling my responsibilities to NCI.

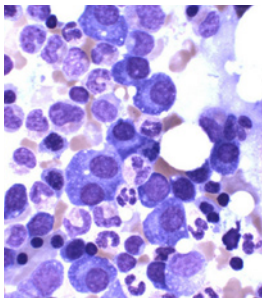
Change is never easy, but with good people and a dedication to success, I have no doubt we can come through it for the better. ◆

Dr. Andrew C. von Eschenbach
Director, National Cancer Institute

Spotlight

Multiple Myeloma: Disease and Treatment

In June of this year, NCI's Press Office hosted a Science Writers' Seminar on the blood-borne cancers: leukemia, lymphoma, and multiple myeloma. While progress has been made in treating many types of leukemia and lymphoma, multiple myeloma remains resistant.



In bone marrow, multiple myeloma produces binucleate plasma cells and cells with enlarged nucleoli.

Multiple myeloma is caused by plasma cells—a type of white blood cell—forming tumors in bone marrow. This disease affects about 16,000 people in this country each year. While the cause is not known, this disease is most prevalent in the elderly, suggesting it may be related to a decline in the immune system with aging.

"Blood plasma cells typically make up less than 5 percent of the cells in the bone marrow," says Dr. Wyndham Wilson of the Lymphoma Therapeutics Section of the Metabolism Branch in NCI's Center for Cancer Research (CCR). "In multiple myeloma, tumor cells are overproduced and can make up between 10 to 80 percent of the cells in the bone marrow, crowding out the normal cells."

Because the normal bone marrow cells are displaced, multiple myeloma patients often suffer from anemia and decreased resistance to infection. Kidney damage can occur as a result of excessive myeloma protein or calcium (from bone destruction) in the blood. This may lead to weakened muscles, malaise, and fatigue. The tumor growth can form multiple bone lesions, usually in the pelvis, spine, ribs, and skull.

Patients are often initially treated with chemotherapy accompanied by support for anemia, renal failure, osteoporosis, bone pain, and infections. About 50 to 75 percent of patients respond to treatment for 2 to 3 years, but all eventually relapse. Following relapse, therapy may include high-dose chemotherapy followed by a bone marrow transplant, which can sometimes extend survival 4 to 5 years.

"We're always looking for new treatments that will improve outcomes," says Dr. Wilson. "There are some promising new drugs being tested in clinical trials, but we're also finding new uses for some old drugs."

One such drug is thalidomide, which was introduced in the 1950s as a sedative and treatment for morning sickness. However, after its use was linked to birth defects, it was withdrawn from the market. Thalidomide has now reemerged and is considered the first new agent to treat multiple myeloma in more than 30 years. Thalidomide is used alone and in combination with other drugs, but many patients experience side effects such as severe numbness and tingling in the limbs. As a result, researchers are exploring similar agents that have fewer adverse effects. Recent clinical trials are evaluating lenalidomide (Revlimid), a derivative of thalidomide. Like thalidomide, it inhibits the growth of myeloma cells and formation of new blood vessels. The FDA granted a fast-track review to evaluate its effectiveness for treatment of multiple myeloma and other blood cell disorders known as myelodysplastic syndromes.

In 2003, FDA approved another new class of cancer drugs known as proteasome inhibitors for treatment of recurrent myeloma. Bortezomib (Velcade) blocks the action of proteasomes, enzyme molecules that regu-

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For more information about multiple myeloma and other cancers of the blood, go to NCI's *BenchMarks* Web site at http://www.cancer.gov/newscenter/benchmarks-vol5-issue3.

The *BenchMarks* site highlights the research featured at the NCI Science Writers' Seminars. New articles are posted every 2 to 3 months. The *BenchMarks* site also features background information on selected cancer topics, along with photos, videos, and animated graphics. The "Science Behind the News" series features tutorials for educational use by life science teachers, medical professionals, and the interested public. They are available in PDF and PowerPoint formats that may be downloaded from the Web. ◆

Cancer Research Highlights

Model Estimates Risk of Breast Cancer Among Survivors of Hodgkin Lymphoma

Researchers have developed a model for estimating a woman's risk of developing breast cancer after being treated with large-field chest radiotherapy for Hodgkin lymphoma (HL). Using the model, they determined that the cumulative absolute risk of breast cancer among female HL survivors increases with age at the end of follow-up, time since diagnosis, and radiation dose.

Breast cancer is the most common solid tumor among young women who survive HL, but individualized risk projections of cumulative absolute risk had not previously been developed. Projections could be used to counsel HL survivors and plan long-term management and prevention strategies.

To create the model, a team led by Drs. Lois B. Travis and Mitchell H. Gail of NCI analyzed data from an international population-based, case-control study of nearly 3,800 female HL survivors who were diagnosed at age 30 or younger. Among the survivors, 105 developed breast cancer, according to findings in the October 5 *Journal of the National Cancer Institute*.

Because the study included women diagnosed from 1965 through 1994, the model is most appropriate for survivors who received HL treatments commonly used in the past. The researchers urge caution in applying the findings to women treated with newer therapies, such as limited-field radiotherapy or ovary-sparing chemotherapy.

Gains in long-term survival provided by radiation therapy and chemotherapy should always be balanced against the associated risks of secondary cancers and other late sequelae, the researchers note. The risk projections will "serve as a unique and valuable resource for the large number of current HL survivors given therapeutic regimens of the past," they write.

Regimen Protects Against Graft-Versus-Host Disease

A new regimen that had previously been tested only in mice has proved effective in helping humans avoid graft-versus-host disease (GVHD). Results of a study by researchers at Stanford University appear in the September 29 *New England Journal of Medicine*.

Normally, people with lymphoid malignant diseases or acute leukemia can be treated with bone marrow transplants after being prepped with high doses of chemotherapy. But 20 to 65 percent of bone marrow transplant patients develop acute GVHD, an illness in which the new, transplanted immune cells attack recipients' skin, intestines, and liver. GVHD causes nearly half of deaths among those who never relapse.

In this study, researchers gave 37 transplant recipients 10 doses of total lymphoid irradiation at 80 cGy per day, starting 11 days before their transplants. The patients then received antithymocyte globulin, as well as immunosuppressive therapy with cyclosporine and mycophenolate mofetil.

After a mean follow-up of 446 to 482 days, only 2 of the 37 patients developed acute GVHD. This incidence is much lower than that cited in the medical literature. It is also striking in that 14 of the participants received transplants from unrelated donors, a situation that normally results in GVHD more than half of the time. In addition, nearly all of the patients who entered the trial in partial remission ended up in full remission after receiving the treatment.

Hitchhiking Viruses Battle Cancer in Mice

While gene therapy originally showed great promise for cancer treatment, the difficulty in delivering therapeutic genes to the growing tumor has hamstrung this technique. Now, a team from the Mayo Clinic reports that hitchhikers can help. By attaching these genetically modified viruses to immune T cells, the team obliterated tumors in mice.

"We use immune cells to home in on the tumors," said Dr. Richard Vile, lead author on the paper published September 18 in *Nature Medicine* online. "There they can deliver whatever therapeutic genes we want."

Dr. Vile explained that as the body defends itself against a growing tumor, T cells begin to recognize and target cancer cells. Ideally, clinicians could remove these cells from the blood, attach beneficial viruses, and return hundreds of thousands of the hitchhiker-rich T cells to the patient.

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As a proof of concept, the team generated T cells designed to home in on a particular type of laboratory-grown mouse tumor similar to melanoma. They then attached a variety of viruses to the T cells and returned the cells to the mice. Between 5 and 14 percent of the injected T cells homed in on the tumors, a rate that Dr. Vile described as "very promising." All of the mice receiving hitchhiker viruses engineered to produce interleukin-12—a growth factor that boosts the immune system—were cured of their tumors.

Because the viruses ride into the tumor on immune system cells, they enjoy a "privileged status" that prevents them from being recognized and destroyed by other immune cells.

Plant Compounds May Reduce Lung Cancer Risk

A large chemoprevention study of phytoestrogens—plant-derived compounds found in many foods—has shown that high intake of the compounds decreases the risk of lung cancer. In the September 28 *Journal of the American Medical Association,* investigators reported that study participants who ate the most phytoestrogens reduced their lung cancer risk by 46 percent compared with those who ate the lowest amount.

Dr. Margaret Spitz, the lead investigator of the study at the University of Texas M.D. Anderson Cancer Center, said that phytoestrogens latch onto estrogen receptors in lung tissue, which, via biomolecular machinery, may explain the reduction in lung cancer risk. But she could not say why women, in general, seemed to benefit less than men from phytoestrogens or why former smokers seemed to benefit less than people who never smoked.

Between 1995 and 2003, the research team enrolled 1,674 patients treated for lung cancer and 1,735 healthy controls. The participants answered detailed questions about their diet for the year before their enrollment or their cancer diagnosis.

The researchers then analyzed consumption of categories of foods that contain different kinds of phytoestrogens: isoflavones (soybeans and soy products, chickpeas, and red clover), lignans (rye grains, linseeds, carrots, spinach, broccoli, and other vegetables), and coumesterol (beans, peas, clover, spinach, and sprouts).

The investigators cautioned that much more research is needed to prove a definitive chemoprevention effect. For example, for reasons not fully understood, high consumption of phytoestrogens did not reduce lung cancer risk in those people studied who had smoked and then quit. "We are just at the beginning of our work to explore the connection between these nutrients and lung cancer risk," said Dr. Spitz.

National Trial Next Step Toward Early Detection of Recurrent Ovarian Cancer

NCI has launched a national clinical trial designed to collect blood samples from patients after successful treatment of advanced ovarian cancer in order to develop an approach for detecting ovarian cancer at an early stage if the disease returns. The trial, led by the Center for Cancer Research (CCR), NCI's intramural research program, will involve 10 additional institutions where a series of blood samples will be collected from women with advanced-stage ovarian cancer who show no signs of cancer after completing their first program of chemotherapy treatment.

"If we can harness all of the protein information in the blood in our patients' samples, we may have a strong lead on how to detect ovarian cancer at an early stage when it can be most effectively treated," said the study's principal investigator, Dr. Elise Kohn of CCR.

Currently the only approved test to determine ovarian cancer recurrence is CA-125 (a test for a protein that is detectable in 80 percent of advanced-stage patients with epithelial ovarian cancer). But the CA-125 test fails to reliably diagnose women who have no signs of recurrence. Advanced-stage cancer has a high likelihood of returning within 3 years of initial treatment, even in the absence of symptoms of recurrence.

The long-term goal of the trial—which will enroll 400 women over 24 months—is to develop an approach to predict the presence of early-stage ovarian cancer using new technology that looks for protein patterns or protein fragments in blood.

"A pilot study launched in 2000 gave us a better understanding of the complexities of protein analysis and reinforced the importance of collecting and analyzing a large number of blood samples and their protein patterns," Dr. Kohn said.

For additional information, go to http://www.cancer.gov/newscenter/pressreleases/OvarianMultiInstituteTrial. ◆

Cancer Awareness in October

A presidential proclamation for National Breast Cancer Awareness Month for October was issued on October 1. For more information on breast cancer, go to http://www.cancer.gov/cancertopics/types/breast. ◆

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late cell growth by breaking down proteins within cells. Bortezomib directly inhibits myeloma tumor cells, but also affects other bone marrow cells and pathways regulating cell growth and survival. Normal cells recover from treatment with bortezomib, while myeloma cells usually die. Recent clinical studies suggest that bortezomib might increase patient survival and be used as a first-line treatment for multiple myeloma.

"Both lenalidomide and bortezomib represent a new approach to the treatment of multiple myeloma," notes Dr. Wilson. "By targeting both the tumor cell and the bone marrow microenvironment, we can treat patients who have developed drug resistance. This may represent a new frontier for treating other blood cancers, such as lymphoma." ◆

By Lynette Grouse

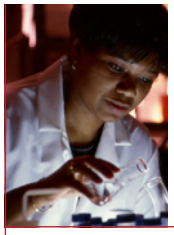
CCR Grand Rounds

October 11: Dr. Phillip A. Sharp, Director, McGovern Institute for Brain Research, Center for Cancer Research, Massachusetts Institute of Technology; "The Surprising Biology of Short RNAs"

October 18th: No Lecture. NIH Research Festival October 17–21

October 25: Dr. Angela Brodie, Professor of Pharmacology and Experimental Therapeutics, Department of Pharmacology, University of Maryland School of Medicine; "Aromatase Inhibitors and Breast Cancer: Concept to Clinic"

CCR Grand Rounds are held 8:30 to 9:30 a.m. at the NIH campus in Bethesda, Md., in the Clinical Center's Lipsett Amphitheater. ◆



Featured Clinical Trial

Milk Thistle Extract for Chemotherapy-Induced Liver Toxicity

Name of the Trial
Phase II Randomized Pilot Study of Silymarin (Milk Thistle Extract) in Patients with Acute Lymphoblastic Leukemia Receiving Hepatotoxic Chemotherapy (CPMC-IRB-14117). See the protocol summary at http://cancer.gov/clinicaltrials/CPMC-IRB-14117.

Principal Investigator
Dr. Kara Kelly, Herbert Irving Comprehensive Cancer Center at Columbia University and the Children's Oncology Group

Dr. Kara Kelley

Why Is This Trial Important?
Acute lymphoblastic leukemia (ALL) is the most common form of cancer in children. Treatment of childhood ALL is usually done in three phases: an induction phase to bring about a major remission of the cancer, a consolidation phase to kill any remaining cancer cells, and a maintenance phase to kill any cancer cells that may regrow.

Although necessary, many chemotherapy drugs used to treat ALL cause harmful side effects, including liver damage. Consequently, treatment doses must often be reduced or withheld.

In this trial, researchers are testing the ability of a nutritional supplement called silymarin to treat liver damage caused by chemotherapy for ALL. Silymarin is an extract of the milk thistle plant and has been shown in laboratory and animal studies to protect the liver from certain toxic chemicals.

"We observed that some parents of children undergoing treatment for ALL were using milk thistle supplements to lessen the effects of liver toxicity, in some cases with noticeable improvement," said Dr. Kelly. "With this trial, we are trying to verify milk thistle's efficacy in reducing chemotherapy-related liver toxicity.

"Additionally, we are exploring the interaction between milk thistle supplements and the chemotherapy drugs used to treat ALL, and so far we have found no evidence of an adverse interaction."

Who Can Join This Trial?
Researchers seek to enroll 50 patients aged 2 to 21 with ALL who are receiving maintenance phase chemotherapy. See the list of eligibility criteria at http://www.cancer.gov/clinicaltrials/CPMC-IRB-14117.

Where Is This Trial Taking Place?
Multiple study sites in the United States are recruiting patients for this trial. See the list of study sites at http://www.cancer.gov/clinicaltrials/CPMC-IRB-14117.

Contact Information
See the list of study contacts at http://www.cancer.gov/clinicaltrials/CPMC-IRB-14117 or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). The call is toll free and completely confidential. ◆

An archive of "Featured Clinical Trial" columns is available at http://cancer.gov/clinicaltrials/ft-all-featured-trials.

Notes

REMBRANDT Team Awarded Service Medal

Dr. Subhashree Madhavan of NCI's Center for Bioinformatics and her colleagues on the REMBRANDT Project received a 2005 Service to America Medal ("Sammie"). They were honored in the category of Science and Environment for developing a national database that will house molecular and genetic data on all types of brain tumors, including information from an NCI clinical study and a vast store of existing information on brain tumors. Conducted in partnership with the National Institute of Neurological Disorders and Stroke, REMBRANDT (REpository for Molecular BRAin Neoplasia DaTa) supports analysis of clinical and molecular datasets from the Glioma Molecular Diagnostic Initiative, a brain tumor study spearheaded by Dr. Howard Fine of NCI's CCR. The Sammies were created in 2002 to recognize the finest achievements of public servants across the country. The medal was awarded on September 28.

Nancy G. Brinker Receives 2005 Lasker Public Service Award

Nancy G. Brinker was awarded the 2005 Lasker Public Service Award on September 18 for creating the Susan G. Komen Breast Cancer Foundation and increasing public awareness about a disease that was once talked about only in whispers and rarely in public. With just $200, Ms. Brinker started the Komen foundation in 1982, 2 years after her sister, Susan Komen, had died of breast cancer at age 36. Today the foundation has more than 75,000 volunteers and has raised more than $740 million to support breast cancer research, education, screening, and treatment. Hundreds of thousands of runners participate in its annual "Race for the Cure," and breast cancer is now understood by the public to be one of the leading causes of death in women. Ms. Brinker started and "nurtured the grass-roots breast cancer advocacy movement," the Lasker Foundation said. Now 58, Ms. Brinker is also a breast cancer survivor.

NCI Funds Centers of Cancer Nanotechnology Excellence

NCI has established seven Centers of Cancer Nanotechnology Excellence (CCNEs) and awarded them a total of $26.3 million in the first year. CCNEs are multi-institutional hubs that focus on integrating nanotechnology into basic and applied cancer research to develop new tools for preventing, diagnosing, detecting, and treating cancer. Each of the CCNE awardees is associated with one or more NCI-designated Cancer Centers, is affiliated with schools of engineering and physical sciences, and is partnered with nonprofit organizations or private sector firms with the intent of advancing the technologies being developed. Nanotechnology is the development and engineering of devices so small that they are measured on a molecular scale. The establishment of these Centers of Excellence is one of four major program components of the NCI Alliance for Nanotechnology in Cancer, a $144.3 million, 5-year initiative launched in 2004. For a list of the CCNEs, go to http://nano.cancer.gov.

Weingarten Joins OTIR as Small Business Program Manager

Michael Weingarten recently joined NCI's Office of Technology and Industrial Relations as small business program manager. As such, he will lead program activities of the Center for Strategic Scientific Initiatives, including policy development and management of NCI's small business programs and strategic partnerships. Before joining NCI, Mr. Weingarten worked for more than 14 years at the National Aeronautics and Space Administration, most recently as a manager in the Exploration Systems Research and Technology Program, where he led a team of experts in forging partnerships with the biomedical industry to develop technologies with implications for national public health. ◆

NCI Listens and Learns

NCI would like to know:

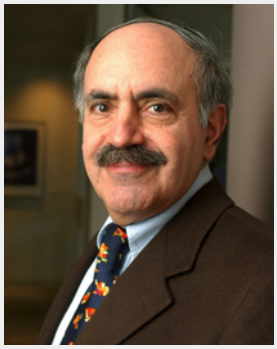
1. What steps should a person looking to join a cancer treatment trial take to find the right trial? Where or to whom should they go for information?
2. The NCI Web site features a "How to Find a Cancer Treatment Trial" guide. NCI would appreciate feedback about the guide's usefulness and relevance.

Please visit the guide and tell NCI:

- Are the steps sufficiently "actionable?" Does the guide empower users to perform the tasks to find a trial?
- What specific improvements should be made to the guide?
- Should this guide be recommended to others?

Go to http://ncilistens.cancer.gov to register and post your comments. ◆

A Conversation with... Dr. Robert Weinberg



Dr. Robert Weinberg is a founding member of the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology. His lab has pioneered discoveries in cancer biology since the late 1970s, including the first human oncogene and the first tumor suppressor gene. He was awarded the National Medal of Science in 1997. On September 28, he discussed "Mechanisms Leading to the Formation of Human Malignancies" in the Stars in Nutrition and Cancer lecture series at NIH.

What is your lab's current model of cancer formation and metastasis?

This is the last frontier of cancer research, but we have a good rough map of the territory. Earlier work with the telomerase gene allowed Vogelstein in 1989 to diagram the five signaling pathways normal human cells must navigate to become tumorigenic. Along the way, they accumulate gene mutations in a process that is very much driven by Darwinian evolution, played out in the microcosm of the body's tissue.

Metastasis is a critical issue in cancer because 9 of 10 cancer deaths are due to distant metastases, not to the primary tumor. Once a small cluster of cells has reached a distant site, the transition from microscopic to macroscopic metastasis occurs very inefficiently. Perhaps only one in a million cancer cells will be the progenitor of an ultimate, possibly life-threatening, macro-metastasis. We are studying four different transcription factors that we believe can program the invasiveness of primary tumor cells that allows them to metastasize: Twist, Slug, Mesenchyme Forkhead, and Goosecoid. Each of these, which is normally active during early embryonic development, has the ability to force cells to become invasive and metastatic.

What role do you see for nutrition in cancer prevention?

It is clear that far more people could avoid cancer by following the precepts developed here at the Division of Cancer Prevention than could ever be saved by even the most successful therapies. I find it quite remarkable that body mass index has such a high positive correlation with the incidence of many types of cancer. The American Cancer Society estimates that 90,000 cancer deaths a year are attributable to obesity. I think it's plausible that insulin-like growth factors present in elevated concentrations in the blood of the obese perturb the biology of cells throughout the body and inhibit their natural death. This could lead in turn to their developing into cancer cells.

What does the future look like for cancer biology?

We know that each of the 110 major types of human cancer has its own genetic biography, its sequences of accumulated genetic changes. The question is whether certain laws will emerge that enable us to rationalize why these changes occur in all of these types of cancer cells. I do expect that the molecular and genetic mechanisms that we and others are uncovering will eventually coalesce into a set of rules that explain how all types of cancer arise. This holds the prospect of making cancer research into a logical, rigorous science rather than just a collection of diverse phenomena that are only described without being understood. ◆

Featured Meetings and Events

A calendar of scientific meetings and events sponsored by the National Institutes of Health is available at http://calendar.nih.gov/cgi-bin/calendar. ◆

The *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads the national effort to eliminate the suffering and death due to cancer. Through basic, clinical, and population-based biomedical research and training, NCI conducts and supports research that will lead to a future in which we can identify the environmental and genetic causes of cancer, prevent cancer before it starts, identify cancers that do develop at the earliest stage, eliminate cancers through innovative treatment interventions, and biologically control those cancers that we cannot eliminate so they become manageable, chronic diseases.

For more information on cancer, call 1-800-4-CANCER or visit http://www.cancer.gov.

NCI Cancer Bulletin staff can be reached at ncicancerbulletin@mail.nih.gov.